

### **REMARKS**

Claims 1, 2, 4, 6, 7, 9 and 11-15 are currently pending and under examination in this application. With this response, claim 1 has been amended to replace the recited ratios and amounts with information about combination index (CI). Support for this amendment can be found throughout the specification and at, for example, page 42, paragraph 136; page 48, the last line of the paragraph directly below Table 7; and the tables in Figures 7A-H, particularly the shaded rows (or the boxed rows as in the published application, US 2005/0191375) therein. New claims 33 and 34 have been added to include the features removed from claim 1. Claim 11 has been amended for this claim to have proper antecedent basis. Applicants respectfully request entry of the claims as amended and examination of the application in light of the following remarks.

#### **I. TELEPHONE INTERVIEW**

Applicants' agent would like to thank Examiners Carter and Padmanabhan for the opportunity to discuss the obviousness rejection in the pending Office Action on October 19, 2010. In the interview, the U.S. Court of Appeals for The Federal Circuit's reasoning in case *In Re Sullivan*, 498 F.3d 1345 (2007) was discussed. In accordance with the Court's directive to the USPTO in *In Re Sullivan*, the undersigned counsel requests that the Examiners give meaningful consideration to the rebuttal arguments provided by the Applicants in regard to the unexpected properties (i.e., anti-inflammatory and synergistic properties) of the composition claimed. During the interview, the Examiners agreed that the unexpected properties of the claimed composition may be sufficient to overcome the prior art. However, Examiner Padmanabhan stated that the specification may not be commensurate in scope with what has been claimed in claim 1, in particular with regard to the recited ratios, amounts, and the methylxanthine genus, and suggested appropriate amendments to the claims be implemented before the next examination. Applicants believe there was substantial progress made during the interview in explaining the claimed invention and in appreciating the Examiner's concerns. Applicants submit that the above claim amendments and following remarks fully address specific points raised

during the interview and in the outstanding Office Action and place the application in condition for allowance.

## **II. CLAIM REJECTIONS UNDER 35 USC § 103**

Claims 1, 2, 4, 6, 7, 9 and 11-15 stand rejected under 35 USC § 103 (a) as being unpatentable over Ramirez (U.S. 2002/0102345) in view of Todd, Jr. et al. (U.S. 5,041,300).

The Action states that Ramirez teaches a beverage composition comprising beer and caffeine (a methylxanthine). The Action acknowledges that Ramirez does not teach dihydroisoalpha acid, but contends that Todd et al. teach the addition of dihydroisohumulone to beer to provide desired flavor. The Action concludes that one skilled in the art would have found it obvious and motivated to combine the composition of Ramirez in view of Todd and the amount of the dihydro-isohumulone and methylxanthine as well as the ratio between the two compounds as disclosed in claims 1, 9 and 11-13 because one skilled in the art would be able to adjust the amounts of these compounds in order to provide the desired effect of aroma and flavor (dihydro-isohumulone) and energy boost (methylxanthine; caffeine). See Office Action, page 4, last paragraph.

The Action further states that in regards to the use of the composition claimed for the treatment of inflammation and the composition having “anti-inflammatory” synergistic amounts, the intended use does not merit patentable weight. Office Action, page 5, first paragraph. Applicants respectfully disagree.

As discussed in the interview, in accordance with the Federal Circuit’s reasoning in *In Re Sullivan (id.)*, while a statement of intended use may not render a known composition patentable, the claimed composition was not known (as the claims are not being rejected under 35 U.S.C. 102), and whether it would have been obvious depends

upon consideration of the evidence including any unexpected properties of the claimed composition.

Applicants submit that the claimed composition has the unexpected property of reducing inflammation as well as exhibiting that RIAA and methylxanthine can act synergistically over all ratios tested albeit at different amounts in these ratios, *i.e.*, when the combination index of the components is less than 1. See page 42, paragraph 136; page 48, the last line of the paragraph directly below Table 7; and the shaded or boxed rows in the tables shown Figures 7A-H.

Applicants further submit that in accordance with the obviousness standards set forth in *KSR*, a person of ordinary skill in art of beer brewing, who was familiar with the teachings of Ramirez and Todd et al., could not have expected or predicted that the combination of RIAA and methylxanthine is effective to treat inflammation and that the combination acts synergistically to do so. As such, Applicants respectfully request that the rejection under 35 USC § 103 be withdrawn.

### **III. ISSUES RAISED DURING THE INTERVIEW**

#### **A. Whether the Specification is Commensurate in Scope with the Claims**

In response to Examiner's concern that the enablement provided in the specification may not be commensurate in scope with what has been claimed relating to the unexpected properties of the composition, Applicants submit that claim 1 as amended renders the ground for such concern moot for the following reasons.

##### **1. Inclusion of Combination Index (CI) in Claim 1**

Applicants submit that the recitation of "Combination Index (CI) of less than 1" as measure of synergistic effects of the composition in claim 1 has been fully disclosed in the specification in both theory and by way of examples. See page 42, paragraph 136; Example 4; page 48, the last line of the paragraph directly below Table 7; last column of

Table 7; and the shaded or boxed rows in the tables shown Figures 7A-H. As such, Applicants submit that the scope of enablement provided to one of skill in the art in the specification is commensurate with the scope of protection sought by the claims.

Applicants further submit that because the “combination index (CI) of less than 1” is both a measure of synergy and a measure for amounts and/or ratios of RIAA and methylxanthine at which such synergy is observed for treating inflammation, the recitation of ratios or amounts in claim 1 was redundant and no longer necessary. As evidenced by the Chou et al. (*J. Biol. Chem.* 252:6438-6442 (1977), see reference C14 in IDS filed 06/26/2009), calculation of combination index takes into account the concentrations of the compounds being tested for synergy. Therefore, to one of ordinary skill in the art of drug development, a “combination index of less than one” is necessarily inclusive of amounts and ratios in which synergy is observed. Applicant submit that based on the teachings of the present application (See page 42, paragraph 136; page 48, the last line of the paragraph directly below Table 7; last column of Table 7; and the shaded or boxed rows in the tables shown Figures 7A-H), a person of ordinary skill in the art can readily and without undue experimentation ascertain the combination index of an RIAA and methylxanthine composition at which the two constituents. Furthermore, by knowing that at a CI of less than one RIAA and methylxanthine act synergistically to treat inflammation, all that a skilled artisan needs to do is to adjust the amounts or ratios of these compounds until a CI of less than one is reached. In other words, the combination index necessarily leads the skilled individual to the amount or ratios at which RIAA and methylxanthine act synergistically.

## **2. Removal of the ratios previously recited in claim 1**

Applicant further submit that the claims are fully enabled in view of the teachings provided in the specification for the unexpected results of synergy. As shown in Table 7, last column and Figures 7A-H, in shaded or boxed rows of the table in these figures, synergy was observed at every ratio of RIAA and caffeine tested (from 100:1 to 1:100 of RIAA to caffeine). Having disclosed that synergy existed over such a wide ratio range

and at every ratio tested, the specification provides that “it is reasonable to expect synergy to occur in vivo over a wide range of doses of both RIAA and caffeine regardless of the ratio of the components in the formulation dosed.” See page 47, paragraph 150, last sentence. Therefore, the specification clearly teaches one of ordinary skill in the art to reasonably expect that the invention as claimed can be practiced without undue experimentation over a wide range of doses of both RIAA and caffeine, not just limited to ratios of 100:1 to 1:100 of RIAA to caffeine. As such, Applicants submit that the unexpected property of the composition disclosed and enabled is commensurate in scope with what is being claimed.

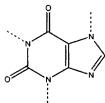
### **3. Removal of the amounts previously recited in claim 1**

As mentioned above, the data in the instant application provides that RIAA and methylxanthine (i.e., caffeine) act synergistically over a wide range of ratios tested albeit at different amounts. Applicants submit that even though synergy has been shown to correspond to the amounts of RIAA and methylxanthine in the composition, the inclusion of the combination index parameter precludes the need to recite any specific amounts in the claims. As discussed above, a “CI of less than one” takes into account the amounts of RIAA and methylxanthines optimal for establishing synergy, and it necessarily excludes any amounts RIAA and methylxanthines that may not provide synergy. As such, Applicants submit that the scope of enablement provided in the specification is still fully commensurate in scope with what has been claimed.

### **4. Whether the Spec. Supports “Methylxanthine” Claimed**

Finally, with regard to the recitation of ‘methylxanthine’ in claim 1, Applicants submit that although specification exemplifies the results of RIAA in combination with only ‘caffeine’, claim 1 is fully supported by the scope of the data provided in the specification because of the following reasons.

Applicants submit that in the application as filed, in Figures 5A-5N, the structures of fourteen methylxanthines have been disclosed, including the caffeine structure which is shown in Figure 5A. As evidenced by these Figures, all methylxanthines share the same core, i.e., a xanthine of structural formula of:



According to the information provided in Wikipedia (a copy of which is enclosed herein), “derivatives of xanthine [which include methylxanthines], known collectively as xanthines, are a group of alkaloids commonly used for their effects as mild stimulants and as bronchodilators, notably in treating the symptoms of asthma.” Considering that there is a presumed expectation that the structurally similar compounds have similar properties, Applicants submit that a person of ordinary skill in the art would have recognized that although the application shows the synergistic anti-inflammatory results of RIAA in combination with caffeine, the same synergistic anti-inflammatory effects must be present in every composition in which RIAA is mixed with a methylxanthine derivatives. In other words, since the interchangeability of xanthin derivatives for different purposes were previously known, the skilled artisan can reasonably predict that the specification is commensurate in scope with what has been claimed as directed to a composition of RIAA and methylxanthine.

Since claim 1 is the only independent claim in this application and all other claims depend from it, the above arguments are also application to all dependent claims. Accordingly, Applicants submit that claims 1, 2, 4, 6, 7, 9 and 11-15 are fully supported by the specification and their practice by one of ordinary skill in the art does not rise to undue experimentation.

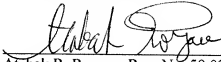
**CONCLUSION**

In light of the amendments and remarks herein, Applicants submit that the claims are in condition for allowance and respectfully request a notice to this effect. If there are any questions regarding these remarks, the Office is invited to contact the undersigned agent at the telephone number provided below.

To the extend necessary, a petition for a three (3) month extension of time under 37 C.F.R. 1.136 up to October 30, 2010, is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to deposit account 50-1133 and please credit any excess fees to such deposit account.

Respectfully submitted,  
McDERMOTT WILL & EMERY LLP

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